

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1.-4. (Canceled).

~~1/5.~~ (~~Previously presented~~) *Actinosynnema pretiosum* strain PF4-4 having ATCC accession number PTA-3921.

~~2/6.~~ (~~Currently amended~~) An enhanced *Actinosynnema pretiosum* strain that produces an ansamitocin in an amount of between about 1.2-fold and about 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565), said enhanced *Actinosynnema pretiosum* strain produced by a method comprising:

- (a) treating a bacterial culture of *Actinosynnema pretiosum* with a mutagen,
- (b) growing the treated bacterial culture of (a) under selective pressure,
- (c) selecting an isolate from the product of (b) that exhibits increased production of an ansamitocin compared with the culture used in (a), and
- (d) optionally repeating (a), (b) and (c) until an isolate that produces between about 1.2-fold and about 10-fold more of an ansamitocin than *Actinosynnema pretiosum* strain N-1231 is obtained.

~~3/7.~~ (~~Previously presented~~) The enhanced *Actinosynnema pretiosum* strain according to claim ~~2~~², wherein the enhanced strain produces an ansamitocin in an amount of between 1.2-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

~~4.~~ ~~(Previously presented)~~ The enhanced *Actinosynnema pretiosum* strain according to claim ~~2~~², wherein the enhanced strain produces an ansamitocin in an amount of between 1.8-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

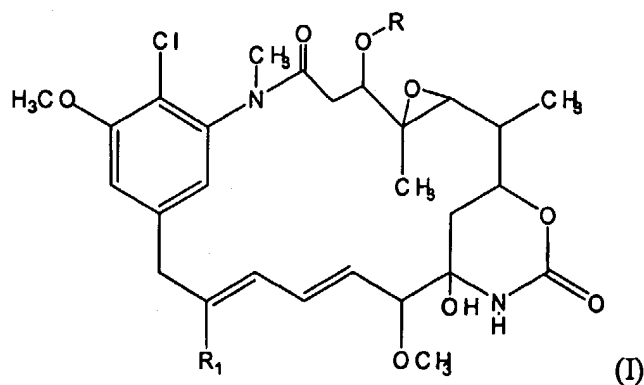
~~5.~~ ~~(Previously presented)~~ The enhanced *Actinosynnema pretiosum* strain according to claim ~~2~~², wherein the enhanced strain produces an ansamitocin in an amount of between 5-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

10. (Canceled).

~~6.~~ ~~(Previously presented)~~ The enhanced *Actinosynnema pretiosum* strain according to claim ~~6~~², wherein the ansamitocin is ansamitocin P-3.

~~7.~~ ~~(Withdrawn)~~ A method for producing an ansamitocin, which comprises cultivating the enhanced *Actinosynnema pretiosum* strain of claim ~~6~~² in a culture medium comprising a suitable carbon source.

~~8.~~ ~~(Withdrawn)~~ The method of claim ~~12~~⁷, wherein said ansamitocin is one or more ansamitocins of formula (I) or isomers thereof:



wherein R is selected from the group consisting of hydrogen, acetyl, propionyl, isobutyryl, butyryl, and isovaleryl, and R₁ is selected from the group consisting of methyl and hydroxymethyl.

~~14.~~ ~~(Withdrawn)~~ The method of claim ~~13~~⁸, wherein R is isobutyryl and R₁ is methyl.

~~15.~~ ~~(Withdrawn)~~ The method of claim ~~12~~², wherein said ansamitocin is ansamitocin P-3 and said carbon source comprises one or more carbon sources selected from the group consisting of valine, isobutyric acid, isobutyl alcohol, and isobutylaldehyde.

16. (Currently amended) An enhanced *Actinosynnema* strain that produces an ansamitocin in an amount of between about 1.2-fold and about 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565), said enhanced *Actinosynnema* strain produced by a method comprising:

- (a) treating a bacterial culture of an *Actinosynnema* strain with a mutagen,
- (b) growing the treated bacterial culture of (a) under selective pressure,
- (c) selecting an isolate from the product of (b) that exhibits increased production of an ansamitocin compared with *Actinosynnema pretiosum* strain N-1231, and
- (d) optionally repeating (a), (b) and (c) until an isolate that produces between about 1.2-fold and about 10-fold more of an ansamitocin than *Actinosynnema pretiosum* strain N-1231 is obtained.

17. (Previously presented) The enhanced *Actinosynnema* strain according to claim 16, wherein the enhanced strain produces an ansamitocin in an amount of between 1.2-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

wherein R is selected from the group consisting of hydrogen, acetyl, propionyl, isobutyryl, butyryl, and isovaleryl, and R₁ is selected from the group consisting of methyl and hydroxymethyl.

23. (Withdrawn) The method of claim 22, wherein R is isobutyryl and R₁ is methyl.

24. (Withdrawn) The method of claim 21, wherein said ansamitocin is ansamitocin P-3 and said carbon source comprises one or more carbon sources selected from the group consisting of valine, isobutyric acid, isobutyl alcohol, and isobutylaldehyde.

25.-33. (Canceled).

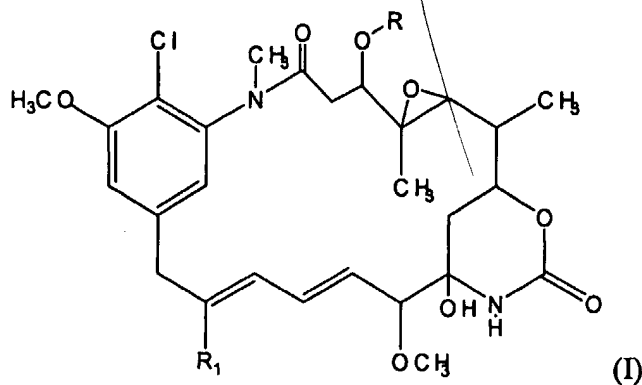
34. (Currently amended) A method of producing an enhanced *Actinosynnema* strain that produces an ansamitocin in an amount of between about 1.2-fold and about 10-fold more than the amount produced by a parental *Actinosynnema* strain from which the enhanced strain is derived, said method comprising:

- (a) treating a bacterial culture of an *Actinosynnema* strain with a mutagen,
- (b) growing the treated bacteria of (a) under selective pressure,
- (c) selecting for an isolate from of the product of (b) that exhibits increased production of an ansamitocin compared with the culture used in (a), and
- (d) optionally repeating (a), (b) and (c) until an isolate that produces between about 1.2-fold and about 10-fold more of an ansamitocin than the culture used in (a) is obtained.

35. (Canceled).

36. (Previously presented) The method of claim 34, wherein said *Actinosynnema* strain is a strain of an *Actinosynnema pretiosum*.

18. (Previously presented) The enhanced *Actinosynnema* strain according to claim 16, wherein the enhanced strain produces an ansamitocin in an amount of between 1.8-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).
19. (Previously presented) The enhanced *Actinosynnema* strain according to claim 16, wherein the enhanced strain produces an ansamitocin in an amount of between 5-fold and 10-fold more than the amount produced *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).
20. (Previously presented) The enhanced *Actinosynnema* strain according to claim 16, wherein the ansamitocin is ansamitocin P-3.
21. (Withdrawn) A method for producing an ansamitocin, which comprises cultivating the enhanced *Actinosynnema* strain of claim 16 in a culture medium comprising a suitable carbon source.
22. (Withdrawn) The method of claim 21, wherein said ansamitocin is one or more ansamitocins of formula (I) or isomers thereof:



37. (Withdrawn) The method of claim 34, wherein the mutagen is UV light or 1-methyl-3-nitro-1-nitroso-guanidine.

38. (Previously presented) The method of claim 34, wherein the enhanced *Actinosynnema* strain produces an ansamitocin in an amount of between 1.2-fold and 10-fold more than the amount produced by the parental *Actinosynnema* strain.

39. (Previously presented) The method of claim 34, wherein the enhanced *Actinosynnema* strain produces an ansamitocin in an amount of between 1.8-fold and 10-fold more than the amount produced by the parental *Actinosynnema* strain.

40. (Previously presented) The method of claim 34, wherein the enhanced *Actinosynnema* strain produces an ansamitocin in an amount of between 5-fold and 10-fold more than the amount produced by the parental *Actinosynnema* strain.

41. (Withdrawn) The method of claim 34, wherein the selective pressure comprises growth of the treated bacteria on CM4-1 media.

42.-49. (Canceled).